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EXAMINER

NGUYEN, QUANG

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/018,392	Applicant(s) KURACHI ET AL.	
	Examiner QUANG NGUYEN, Ph.D.	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 April 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5,6,12,13,15 and 21-30 is/are pending in the application.
- 4a) Of the above claim(s) 3,5,6,22,24 and 25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-2, 12-13, 15, 21, 23 and 26-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Amended claims 1-3, 5-6, 12-13, 15, 21 and new claims 22-30 are pending in the present application.

Applicant's election with traverse of SEQ ID NO:3 as a species of age-regulatory sequence in the reply filed on 4/17/08 is acknowledged. The traversal is on the ground(s) that the Examiner has failed to demonstrate (a) an undue search burden, and b) lack of unity of invention under PCT Rule 13.1. Applicants further argue that the Examiner fails to consider that the **"corresponding special technical feature"** between the sequences is that they each contain the 102-bp stem-loop forming sequence (SEQ ID NO:91), which is contained within the 154-bp SEQ ID NO:93 (AE3"), which in turn is contained within the 1273-nt SEQ ID NO:3 (AE3'); and that the special technical feature defines a contribution which each of the claimed inventions, as a whole, makes over the prior art.

This is not found persuasive for the following reasons.

Firstly, the special technical feature of the instant claims does not rely exclusively on the 102-bp stem-loop forming sequence (SEQ ID NO:91), but also sequences that constitute or define SEQ ID NO:93 (for example see at least claim 3) and SEQ ID NO:3 (for example se at least claim 26).

Secondly, the special technical feature of the present invention also does not define a contribution as a whole makes over the prior art as evidenced by the rejections applied below.

Thirdly, it is undue burden for the examiner to search SEQ ID NO:3, SEQ ID NO:93, SEQ ID NO:91 and specific combinations thereof due to the now very high and continued exponential increase of size of the sequence databases to be searched, resulting in a corresponding increase in computer search time and examiner's time for reviewing the computer search results.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 3, 5-6, 22 and 24-25 were withdrawn from further consideration because they are directed to non-elected species.

Therefore, claims 1-2, 12-13, 15, 21, 23 and 26-30 are examined on the merits herein with the elected species SEQ ID NO:3.

Terminal Disclaimer

The terminal disclaimer filed on 11/02/07 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted for US Application No. 11/129,861 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Response to Amendment

The rejection under 35 U.S.C. 101 because the claims encompass a non-statutory subject matter was withdrawn in light of Applicant's amendment.

The rejection under 35 U.S.C. 112, first paragraph, for Enablement was withdrawn in light of Applicant's amendment.

The provisional rejection under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending Application No. 11/129861 was withdrawn in light of Applicant's submission of the Terminal Disclaimer filed on 11/02/07.

Claim Objections

Claims 12, 23 and 27-28 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. This is because of the limitation **"further comprising"** in these dependent claims, while in the independent claims 1, 23 and 26 from which these dependent claims are dependent on they recite "a recombinant expression vector **consisting of**" and "an age regulatory sequence **consisting of**".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26-27 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 recites the limitation "said recombinant expression vector further comprises" in lines 1-2 of the claim. There is insufficient antecedent basis for this limitation in the claim. This is because in claims 21 and 2 from which claim 29 is dependent on, there is no recitation of any recombinant expression vector. Accordingly, the metes and bounds of the claim are not clearly determined.

The term "substantially purified" in claim 26 is a relative term which renders the claim indefinite. The term "substantially purified" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear to what degree of purification that a nucleic acid sequence can or can not be considered to be "substantially purified".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Amended claims 1-2, 13 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Kurachi et al. (J. Biol. Chem. 270:5276-5281, 1995) as evidenced by Yoshitake et al. (Biochemistry 24:3736-3750, 1985). ***This is a slightly modified rejection.***

With respect to the elected species, Kurachi et al disclose the construction of a set of three human factor IX minigene expression vectors, p-416FIXc, p-416FIXm1 and p-416FIXm2, and the p-416FIXm1 and p-416FIXm2 constructs containing a truncated intron 1 of the factor IX gene showed 7-9 fold higher expression activities than p-416FIXc that does not contain a factor IX intron 1 sequence (see abstract). All of the expression vector constructs contain the human factor IX exon VIII along with 3' flanking genomic sequences and **a minimal human factor IX promoter**, FIX-416/29 promoter sequence (Figure 2; and Materials and Methods section). The human factor IX exon VIII (nucleotides 30822-32757) comprises the 3' UTR having SEQ ID NO:3 (nucleotides 31,418-32,690) as evidenced by the disclosure of Yoshitake et al. (see Figure 3, Table I and the previously attached sequence search). Accordingly, all the expression vector constructs of Kurachi et al. contain the 3' UTR having SEQ ID NO:3. Please note that that **disclosed nucleic acid sequences outside of the sequence consisting of SEQ ID NO:3 in a human factor IX minigene construct can be considered to be parts of a nucleic acid sequence encoding Factor IX protein in the form of a recombinant expression vector or in the form of a transgene**. Furthermore, as defined in the present application the term "expression vector" refers to a recombinant DNA molecule containing a desired coding sequence and appropriate nucleic acid sequences necessary for the expression of the operably linked coding sequence in a particular host organism (page 18, lines 11-13).

Kurachi et al further teach the transfection of HepG2 cells with the aforementioned human factor IX minigene expression vectors (page 5277, right-hand

col., fourth paragraph), and the expression of factor IX in the cell cultures was assayed (Table II and Fig. 4).

Accordingly, the teachings of Kurachi et al meet the limitation of the instant claims as written, and therefore the reference anticipates the instant claims.

Response to Arguments

Applicant's arguments related to the above rejection in the Amendment filed on 11/02/07 (pages 13-14) have been considered but they are respectfully not found persuasive for the following reasons.

Applicants argue basically that Kurachi et al's 3'UTR contained but did not consist of SEQ ID NO:3 (elected species) and that the claims recite "vector consisting of" and "encoding factor IX protein".

As already explained in the above rejection, **disclosed nucleic acid sequences outside of the sequence consisting of SEQ ID NO:3 in a human factor IX minigene construct can be considered to be parts of a nucleic acid sequence encoding Factor IX protein in the form of a recombinant expression vector or in the form of a transgene.**

Accordingly, the teachings of Kurachi et al still meet all limitation of the claims as written, and therefore the reference anticipates the instant claims.

New claim 27 is rejected under 35 U.S.C. 102(b) as being anticipated by Yoshitake et al. (Biochemistry 24:3736-3750, 1985). ***This is a new ground of rejection.***

Due to the open language of "further comprising", which means that additionally sequences can be added to the sequence consisting of SEQ ID NO:1; the following rejection is applied.

Yoshitake et al already disclosed a nucleotide sequence of the gene for human factor IX that has both SEQ ID NO:1 and SEQ ID NO:3 of the present invention in operably linkage (see at least Figure 3).

Accordingly, the teachings of Yoshitake et al meet the limitation of the claim as ambiguously written, and therefore the reference anticipates the instant claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended claims 1-2, 12-13, 15, 21, 23 and 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jallat et al. (US 5,814,716) in view of Yoshitake et al. (Biochemistry 24:3736-3750, 1985) and evidenced by Anson et al. (EMBO J. 3(5):1053-1060, 1984). ***This is a new ground of rejection.***

With respect to the elected species, Jallat et al disclose expression vectors comprising in operable linkage a promoter (e.g., a 5 kb-human factor IX gene promoter), coding sequence for human factor IX (hFIX), and the complete 3' UTR of the hFIX gene, particular the genomic sequence comprising 8 exons and 7 introns described by Anson et al in EMBO J 3:1053, 1984 (see the entire reference, particularly Figs. 2-3; col. 3, lines 8-64; col. 4, line 20 continues to line 10 of col. 5; Examples 1-2). The vectors comprise all of exon 8 of the hFIX gene which includes the 3' UTR that differs from SEQ ID NO:3 of the present invention by three nucleotides at positions 109, 646 and 891 of SEQ ID NO:3 as evidenced by the disclosure of Anson et al. (see at least Figure 4 on page 1057). Jalat et al also teach specifically that a transgenic non-human animal is obtained by the development of an egg which has been injected with a first exogenous DNA fragment comprising a region coding for factor IX and placed under the control of a promoter region specific to the liver such as the 5 kb-human factor IX gene promoter, and that this transgenic animal can cross with a transgenic animal whose genome

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comprises an oncogene sequence placed under the control of a promoter specific to the liver to generate an offspring which is doubly transgenic for the oncogene and factor IX (see col. 3, lines 54-64). Jallat et al further disclose that for the purpose of the described invention, the exogenous DNA fragment must be put into linear form and dissociated from the other plasmid elements (col. 4, lines 59-63).

Jallat et al do not teach specifically the use of an exogenous DNA fragment containing a sequence consisting of SEQ ID NO:3 and/or SEQ ID NO:1, even though Jallat et al disclose specifically the use of an expression block containing a human factor IX gene promoter such as the 5 kb-human factor IX gene promoter, operably linked to a coding sequence for human factor IX (hFIX), and the complete 3' UTR of the hFIX gene for generating at least a transgenic non-human animal.

However, at the effective filing date of the present application, Yoshitake et al already disclosed a nucleotide sequence of the gene for human factor IX that has both SEQ ID NO:1 (present in the 2866-bp promoter region) and SEQ ID NO:3 (present in the 3'UTR) of the present invention in operably linkage (see at least Figure 3).

Accordingly, it would have been obvious for an ordinary skilled artisan at the time of invention was made to modify the teachings of Jallat et al by also utilizing both the human factor IX gene promoter and the complete 3'UTR of the hFIX gene in the human factor IX gene disclosed by Yoshitake et al in an expression vector construct for injecting into a non-human animal egg. Please note that that **nucleic acid sequences outside of the sequence consisting of SEQ ID NO:3 in a modified exogenous DNA fragment resulting from the combined teachings of Jallat et al. and Yoshitake et**

al. can be considered to be parts of a nucleic acid sequence encoding Factor IX protein in the form of a recombinant expression vector or in the form of a transgene.

An ordinary skilled artisan would have been motivated to carry out the above modification because the human factor IX gene of Yoshitake et al has been sequenced and characterized by Yoshitake et al.

An ordinary skilled artisan would have a reasonable expectation of success in light of the teachings of; coupled with a high level of skill of an ordinary artisan in the relevant art.

Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Conclusions

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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/QUANG NGUYEN, Ph.D./

Primary Examiner, Art Unit 1633